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Computational Modeling of Astrocytic Glutamate Input to Neurons

Elizabeth Hansen

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Elizabeth Hansen with Dr. Sheryl Hemkin

QuickTime™ and a
TIFF (Uncompressed) decompressor
are needed to see this picture.

Figure 5

Astrocytes imaged using fluorescent confocal imaging.

Shin, 2005

The Model

To initiate the study of a "dressed" neuron system, the interaction of one astrocyte and one neuron, experimentally derived information was taken from the literature and used to create a model.

The model simulates the changes in the neuron's membrane potential as it is being stimulated by external inputs, ex. glutamate, background "noise."

$$V_{\substack{membrane\\potential}}(t) \;=\; N_{noise}(t) \;+\; G_{glutamate}(t)$$

Stimuli to the Neuron (both new and accumulated signal affects membrane potential) -

N_{noise} = background noise, *guides spontaneous firing rate*

$G_{glutamate}$ = extra-neural glutamate signal, *excitatory neurotransmitter*

The noise term is representative of the inputs acting on the neuron that act as background. They are not signaling, they simply the "noise" associated with the activity in the brain.

The glutamate is the gliotransmitter that we are focusing on. This term represents the potential of the input of glutamate coming to the neuron from the astrocyte. The final part of this equation is the membrane potential. This is the amount of depolarization the neuronal membrane undergoes when external signaling molecules are acting on it.

Another important part of the model is the refractory period. There are, in fact, two refractory periods associated with each input. The absolute refractory period is a time right after the firing of an action potential where another action potential cannot be fired, regardless of its level above threshold. This period can be 1-3 ms in length. Following the absolute refractory period is the relative refractory period. In the relative refractory period an action potential can be\ fired, but it must be a specific amount above threshold. Relative refractory periods can last 3-5 ms. This addition to the model is reflected in the spiking patterns for each input (Fig 1b, Fig 2b, Fig 3c).

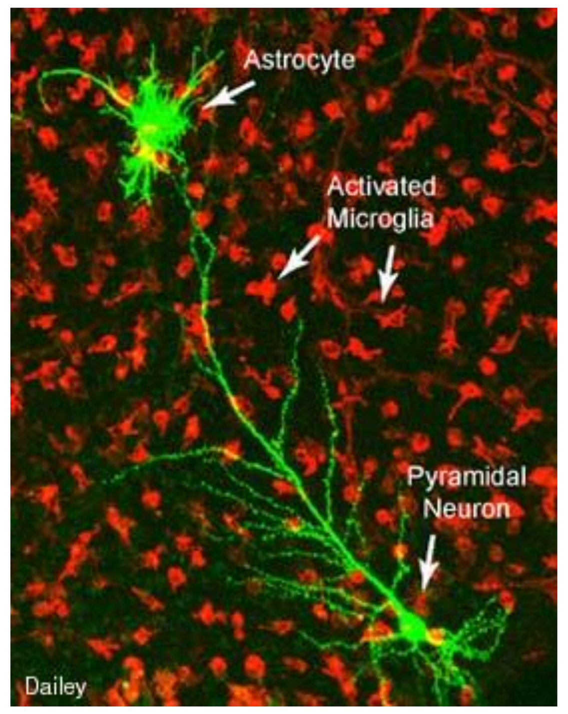


Figure 4

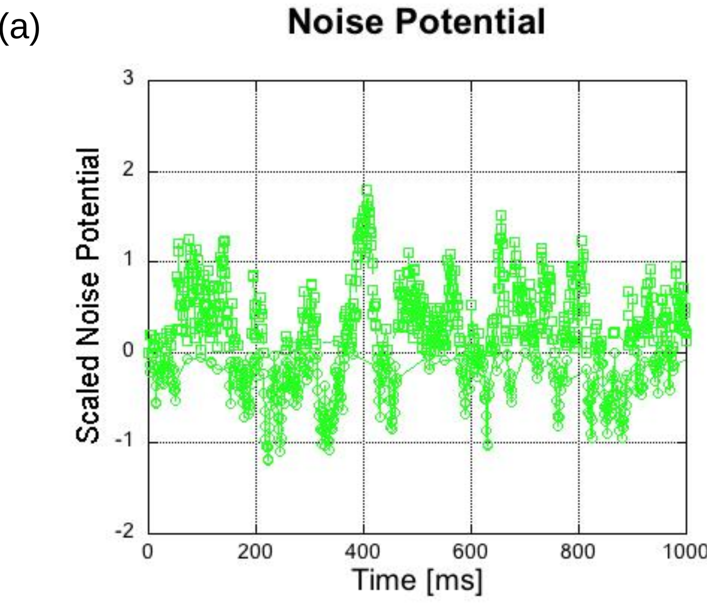
A fluorescent confocal image in live brain tissue slices of the astrocyte and neuron system.

Bedictssen, 2003

Introduction

This project initiated the creation of a physiologically sound model of the communication between neurons and astrocytes. Astrocytes are small, star-shaped glial cells that are located next to the neurons in the brain. Glutamate is an excitatory neurotransmitter that is released from the astrocyte and can diffuse to the membrane of the neuron. The focus of this study was the affect of astrocytic glutamate on the membrane potential of the neuron.

(a)



(b)

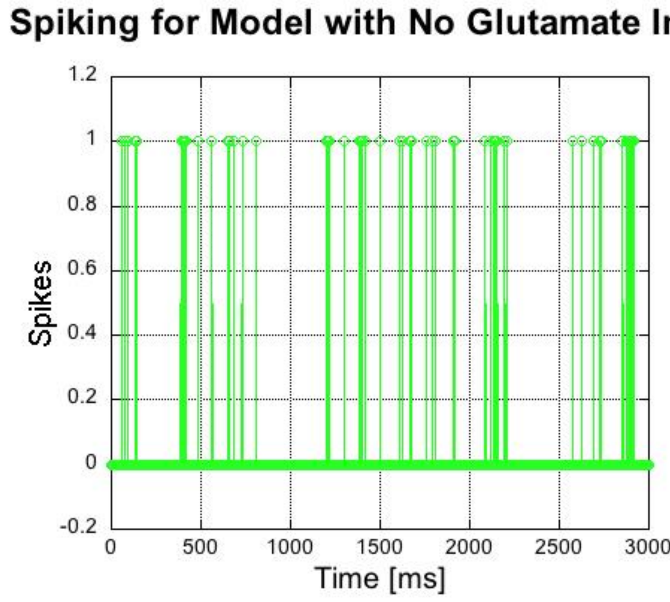


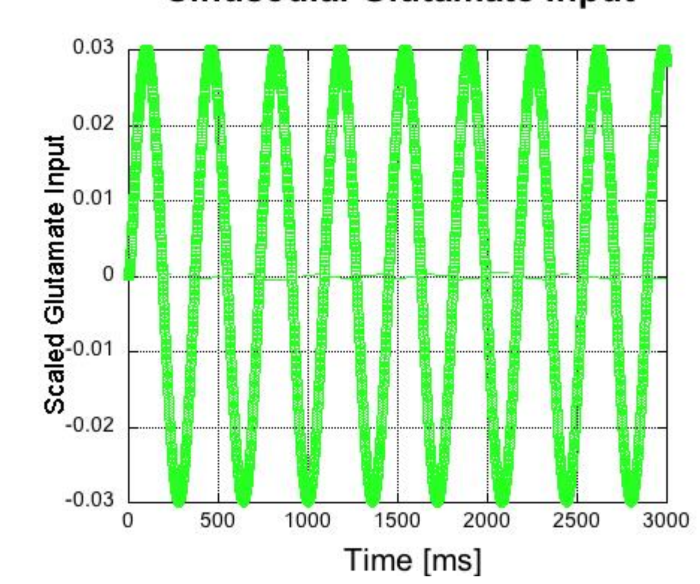
Figure 1

(a) The scaled membrane potential for the noise term over 1000 ms. The noise term was found using the equation:

$$N_{current} = N_{old} \times e^{(-1/D)} + R$$

$N_{present}$ = the membrane potential at the present time
N_{old} = the membrane potential a millisecond before
D = the decay constant specific to the neuron
R = a random number
(b) When the noise potential reaches the threshold an action potential is fired. The spacing between the spikes is due not only to the potential, but also to the refractory periods.

(a)



(b)

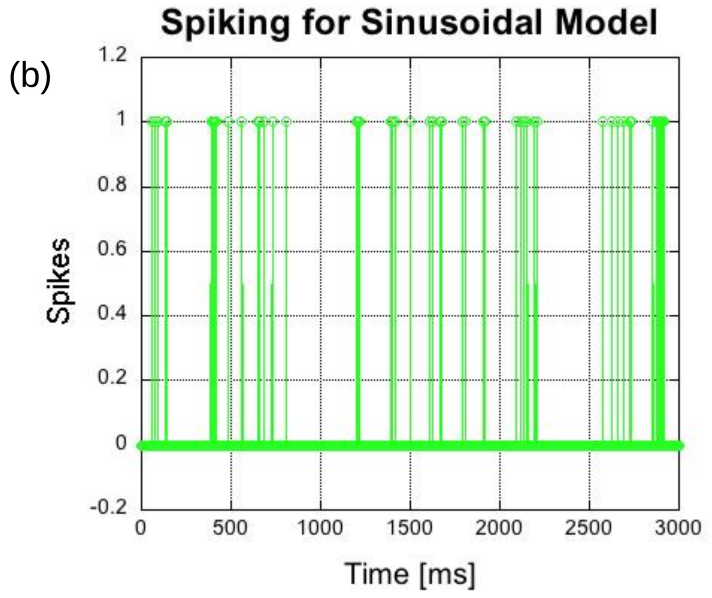


Figure 2

(a) Represents the change in membrane potential that correlates to the sinusoidal model of glutamate input over 3000 ms. The sinusoidal model was used to mimic the oscillatory nature of the glutamate input. The resting potential of this model is scaled to zero (the actual resting potential being -65 mV for a CA1 pyramidal neuron) and the threshold potential has been scaled to one. (b) When the scaled potential reaches threshold or surpasses threshold an action potential is fired.

Acknowledgments:

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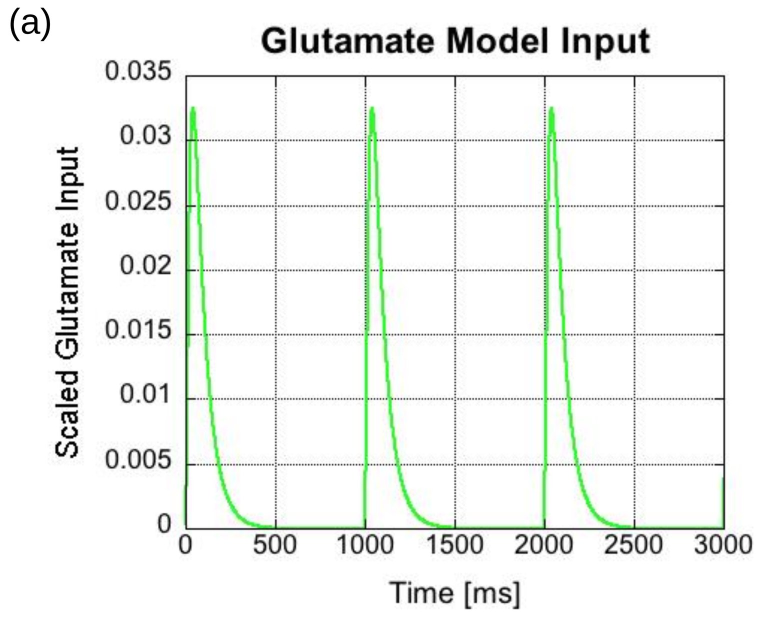
Figure 6

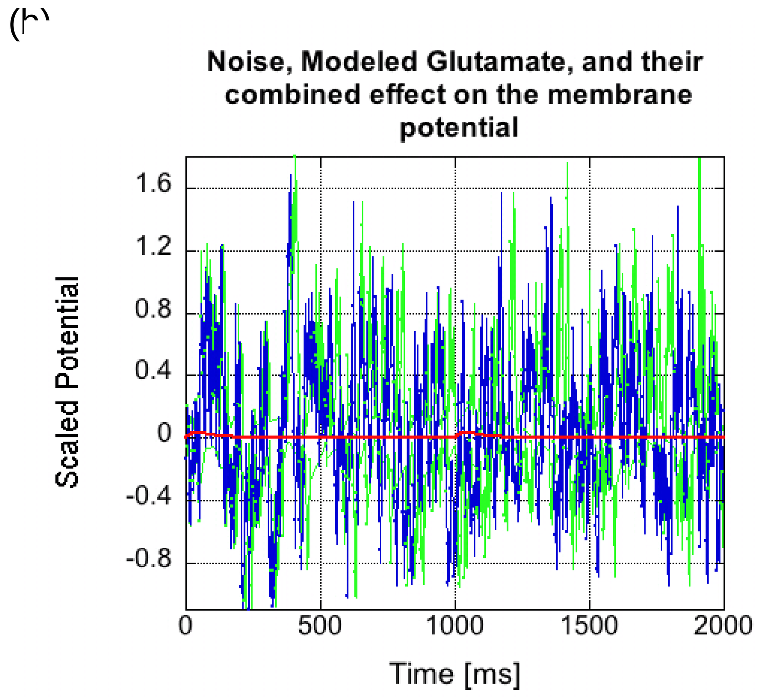
A pyramidal neuron imaged using fluorescent confocal imaging.

Reynolds, 2007

(a)



(b)



(c)

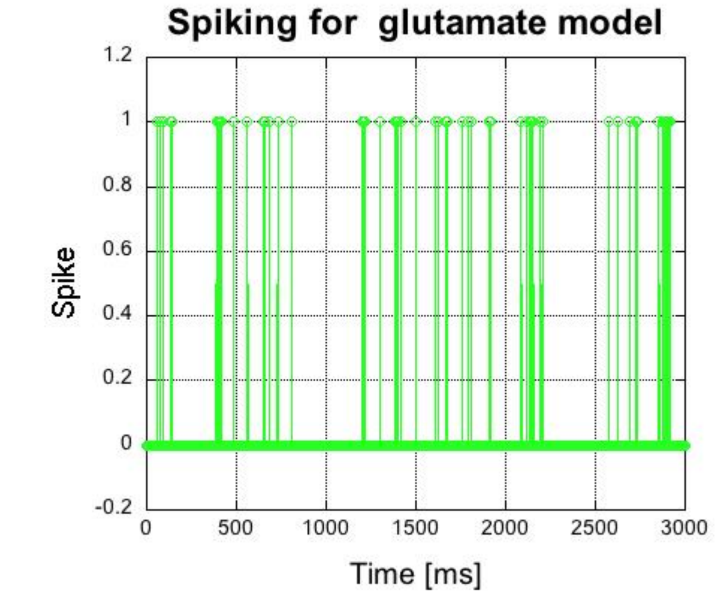


Figure 3

(a) The inset is a recorded EPSP from a neruon. This EPSP was used to model the input of glutamate shown above. Though, not an exact model it is more physiologically sound. (b) The glutamate (in red) seems to be a small, straight line, but when comparing the noise input (in green) to the total change in potential (in blue) it is clear that the glutamate has a marked effect on the total potentiation. (c) This can also be inferred from the spiking of action potentials for the glutamate model.